

AMENDMENTS TO THE SPECIFICATION:

On page 1, 4th paragraph, please replace the following paragraph with the following paragraph listed below:

The findings that mutations in a multitude of oncogenes ~~oneogens~~ and repressor genes of the cells are causally related with the development of tumours, have resulted in a multitude of efforts made to develop selective, cause-oriented chemotherapeutic agents. This involves e.g. inhibitors of farnesyltransferase and ~~tyrosine~~kinase tyrosine kinase inhibitors, gene therapies aimed to restore suppressor gene functions or DNA repair or antisense oligonucleotides against various oncogenes ~~oneogens~~ (e.g. ras, raf, erb). These new cancer targets promising a higher selectivity and efficiency includes also telomerase.

On page 2, 1st paragraph, please replace the following paragraph with the following paragraph listed below:

Its function consists, on the one hand, in protecting chromosome ends against the degradation or fusion – preventing karyotypical changes and genetic instabilities, on the other hand, in counting the number of running cell divisions. The length of telomeric ~~telemerie~~ DNA was found to be between about 1000 and 12000 base pairs (Harley, 1991).

On page 3, 4th paragraph, please replace the following paragraph with the following paragraph listed below:

A therapy directed to inhibit the telomerase activity might have few side effects, excluding human germ cells however. In contrast, stem cells of renewable tissues have longer telomeres than cancer cells and have a lower proliferation rate than cancer cells, which both might protect them against telomere shortening induced by telomerase ~~telemerase~~ inhibitors (Holt et al., 1996). Thus, such an antitelomerase therapy may be regarded as an efficient and selective therapy of malignant tumours which is superior to the present chemotherapy.

On page 4, 1st paragraph, please replace the following paragraph with the following paragraph listed below:

As nucleosides only azidothymidine (AzT) and 2', 3' dideoxyguanosine (ddG) resulted in a shortening of the telomeric DNA in some cell lines, when applied for a longer ~~finger~~ time, however, without changing essentially their growth behaviour or inducing a proliferation stop (Strahl et al., 1996).

On page 4, 2nd paragraph, please replace the following paragraph with the following paragraph listed below:

Furthermore, the telomerase RNA ~~tightly~~ ~~tighty~~ bond to the telomerase Protein was described as another promising target. Thus, antisense oligonucleotides binding complementary to the template region of RNA inhibit the enzyme activity. Indeed, it was shown that permanent inhibition of telomerase in HeLa cells expressing antisense oligonucleotides against template RNA of telomerase caused an increasing shortening of the telomeric DNA which resulted in all death after 23-26 population doublings (Feng et al., 1995).

On page 4, 3rd paragraph, please replace the following paragraph with the following paragraph listed below:

Antisense oligomers in which the sugar phosphate backbone is replaced by N (2-amino ethyl) glycine (peptide nucleic acids, PNA) were described to inhibit the telomerase in vitro at nanomolecular range (Norton et al., 1996). Here again ~~again~~, the template region of telomerase RNA was used as target. However, it is also known from these excellently binding PNAs that they, could not be taken up by cell membranes which ~~whievh~~ limits their applicability (Hanvey et al., 1992). In the same paper Norton et al. reported that oligonucleotides modified by phosphorothioates are efficient, but non-specific inhibitors of telomerase.

On page 5, 3rd paragraph, please replace the following paragraph with the following paragraph listed below:

The invention is implemented according to the claims and based on the surprising finding that the phosphorothioates described do not bind to RNA but sequence-non-specifically to a protein site, called primer binding site which is thought ~~thought~~ to fix the end of telomeric DNA to be elongated. That means, there exist two neighboring targets for telomerase inhibition.

On page 15, 3rd paragraph, please replace the following paragraph with the following paragraph listed below:

Cells of the human tumour cell line HL60 were lysed and a 1000-cell equivalent of this extract was used in the TRAP assay (Telomeric repeat amplification protocol) described by Piatyzek et al. in 1995 for the determination of the efficiency of the two chimeric oligonucleotides nos. 5 and 8 to inhibit telomerase activity. In principle, a radioactively labelled ~~lebeled~~ primer was thereby elongated by the activity of telomerase and the telomerase product formed after PCR amplification and gel electrophoresis was quantitatively evaluated by phosphorus imaging. The oligonucleotides nos. 5 and 8 are in a position to strongly inhibit the activity of telomerase. An inhibition of the telomerase activity by 50 % is reached by oligonucleotide no. 5 at 0.5 nM and by oligonucleotide no. 8 at 1 nM.